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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/506,011	02/17/2000	John Cooper Cox	017227/0155	6856

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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/506,011	COX ET AL.
	Examiner	Art Unit
	Emily Le	1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09/29/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,6-8,12-17 and 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,6-8,12-17 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Art Unit Location

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1648, Examiner Emily Le.

Status of Claims

2. Claims 2, 4-5, 9-11 and 18-52 are cancelled. Claims 1, 3, 6-8, 12-17 and 53 are pending and under examination.

Specification

The disclosure is objected to because of the following informalities:

The use of the trademark ISCOMATRIX ™ has been noted in this application. It should be capitalized wherever it appears **and be accompanied by the generic terminology.**

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Additionally, it is noted that Applicant's 10/13/2002 submission is directed at a substitute specification, as further exemplified by Applicant's 12/17/2002 submission. However, the Examiner cannot locate a substitute specification or find reason(s) as to why a substitute specification is necessary. The Office requests that Applicant clarify the issue.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The enablement rejection directed at claims 6-8 and 53 is withdrawn.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. The 102(a) rejection using Berglindh et al. is withdrawn. Coordinated with the withdrawal of the rejection, any argument(s) and/or affidavit submitted will not be considered.

7. Claims 1, 3, 6-8, 12-17 and 53 are rejected under 35 U.S.C. 102(e) as being anticipated by Drane et al.[1]

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome

either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The claims are directed to a composition comprising a negatively charged organic complex and a positively charged antigen, wherein the organic complex comprises saponin and sterol, and the organic complex and the antigen are electrostatically associated. The claims later limit the antigen to i) comprise a peptide region, or ii) a protein. The claims require the naturally negatively charged organic complex be modified to increase its negativity; and the antigen be modified to increase its positivity. The claims also require the organic complex to further comprise a phospholipids, which is later limited to a phosphoglyceride or lipid A; wherein the phosphoglyceride is selected from the group consisting of phosphatidyl inositol, phosphatidyl glycerol, phosphatidic acid and cardiolipin; and the lipid A is either diphosphoryl lipid A and monophosphoryl lipid A. The claims additionally require the complex to induce a cytotoxic T-lymphocyte response when administered to a mammal.

Drane et al. teaches a composition comprising a negatively charged organic complex and a positively charged antigen. The organic complex of Drane et al. comprises saponin and sterol. Both the organic complex and the antigen of Drane et al. are electrostatically associated with one another. The antigens Drane et al. teaches include both a protein and a peptide region. Drane et al. also teaches enhancing the negativity of the organic complex. Drane et al. additionally teaches enhancing the

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[1] Drane et al., U.S. PreGrant Publication 20040191270, published 09/30/2004; and claims priority to

positivity of the antigen by the addition of positively charged proteins. The organic complex of Drane et al. further comprises phospholipids, specifically phosphatidyl inositol, phosphatidyl glycerol, phosphatidic acid, cardiologic, diphosphoryl lipid A and monophosphoryl lipid A. Lastly, the immunogenic complex of Drane et al. is capable of inducing a cytotoxic T-lymphocyte response when administered to a mammal. [See claims 1 and 44-99]

Drane et al. teaches the claimed invention, including all the limitations recited in the claims. Thus, Drane et al. anticipates the claimed invention.

8. Claims 1, 3, 6 and 12-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Garcon et al.[2]

The claims are directed to a composition comprising a negatively charged organic complex and a positively charged antigen, wherein the organic complex comprises saponin and sterol, and the organic complex and the antigen are electrostatically associated. The claims later limit the antigen to i) comprise a peptide region, or ii) a protein. The claims require the naturally negatively charged organic complex be modified to increase its negativity. The claims also require the organic complex to further comprise a phospholipids, which is later limited lipid A or a phosphoglyceride; wherein lipid A is either diphosphoryl lipid A or monophosphoryl lipid A. The claims additionally require the complex to induce a cytotoxic T-lymphocyte response when administered to a mammal.

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continuation application no. 09/714438, filed on 11/17/2000 and provisional applications 60/166652 and 60/224362, filed 11/19/1999 and 08/11/2000, respectively.

[2] Garcon et al. WO 96/33739, published 10/31/1996

Garcon et al. teaches a composition comprising a negatively charged organic complex and a positively charged antigen. The organic complex of Garcon et al., SUV, comprises saponin and sterol. The sterol that Garcon et al. uses is cholesterol. The organic complex of Garcon et al. has been modified to increase its negativity. Garcon et al. increased the negativity with the addition of MPL, which is monophosphoryl lipid A, which is a phospholipid. Additionally, the organic complex of Garcon et al. further comprises egg yolk phosphatidylcholine, which is a phosphoglyceride, a phospholipid.

The antigen that Garcon et al. teaches is HSV glycoprotein D (gD). HSV glycoprotein D is positively charged protein, which inherently comprise a peptide region. Additionally, the composition of Garcon et al. also induces a cytotoxic T-lymphocyte response when administered to a mammal. [Pages 10-12, in particular.]

It is recognized that Garcon et al. does not explicitly state that the organic complex and the antigen are electrostatically associated, as set forth in the claim. However, it is noted that Applicant defines "electrostaticially associated" as a reference to the organic carrier and the antigen being linked, bound or otherwise associated by means which includes electrostatic interaction. [Paragraph bridging pages 9-10 of the specification.]

In the instant, Garcon et al. states that the antigen is entrapped with the organic complex. The entrapment or encapsulation of the antigen and organic complex allows the two components to associate with one another. Thus, the composition of Garcon et al. does comprise an antigen and an organic complex that are "otherwise associated" to one another.

Additionally, according to Stedman's Medical dictionary, bound is defined as limited, circumscribed; enclosed. Since encapsulation involves enclosure of the antigen within the organic complex, the composition of Garcon et al. does comprise an antigen and an organic complex that are bound to one another. Thus, in view of the insight provided by the specification and the broadest and reasonable interpretation for the term "bound", Garcon et al. does teach a composition comprising an antigen and an organic complex that are "electrostatically associated" with one another.

Because Garcon et al. teaches the same composition as claimed, Garcon et al. anticipates the claimed invention.

Additionally, it is noted that in response to the rejection set forth in the record, Applicant argues that Garcon et al. does not even hint that the antigen is electrostatically associated with the organic complex.

Applicant's submission has been considered but it is not found persuasive for reason(s) set forth in the above immediate paragraphs and summarized below.

It is recognized that Garcon et al. does not explicitly state that the organic complex and the antigen are electrostatically associated, as set forth in the claim. However, it is noted that Applicant defines "electrostaticially associated" as a reference to the organic carrier and the antigen being linked, bound or otherwise associated by means which includes electrostatic interaction. [Paragraph bridging pages 9-10 of the specification.]

In the instant, Garcon et al. states that the antigen is entrapped with the organic complex. The entrapment or encapsulation of the antigen and organic complex allows

the two components to associate with one another. Thus, the composition of Garcon et al. does comprise an antigen and an organic complex that are "otherwise associated" to one another.

Additionally, according to Stedman's Medical dictionary, bound is defined as limited, circumscribed; enclosed. Since encapsulation involves enclosure of the antigen within the organic complex, the composition of Garcon et al. does comprise an antigen and an organic complex that are bound to one another. Thus, in view of the insight provided by the specification and the broadest and reasonable interpretation for the term "bound", Garcon et al. does teach a composition comprising an antigen and an organic complex that are "electrostatically associated" with one another.

9. Claims 1, 3, 7, 12-13 and 17are rejected under 35 U.S.C. 102(b) as being anticipated by MacFarland et al.[3]

The claims are directed to a composition comprising a negatively charged organic complex and a positively charged antigen, wherein the organic complex comprises saponin and sterol, and the organic complex and the antigen are electrostatically associated. The claims later limit the antigen to i) comprise a peptide region, or ii) a protein. The claims require the antigen be modified to increase its positivity. The claims also require the organic complex to further comprise a phospholipid, which is later limited to a phosphoglyceride. The claims additionally require the complex to induce a cytotoxic T-lymphocyte response when administered to a mammal.

[3] MacFarland et al. WO 98/36772, published 08/27/1998.

MacFarland et al. teaches a composition comprising a negatively charged organic complex and a positively charged antigen. The organic complex of MacFarland et al. comprises saponin and sterol. The antigen of MacFarland et al. is a protein, which comprises a peptide region. The antigen of MacFarland et al. has been modified to increase its positivity. The organic complex of MacFarland et al. also comprises a phosphatidyl choline, which is a phosphoglyceride, which is a phospholipid. Additionally, the composition of MacFarland et al. induces a cytotoxic T-lymphocyte response when administered to a mammal. [Pages 11-18, in particular.] Lastly, MacFarland et al. teaches that the organic complex and a positively charged antigen associated and bound to one another. [Lines 20-30 of page 15, in particular.] Thus, the organic complex and a positively charged antigen of MacFarland et al. are electrostatically associated with one another. This interpretation is consistent with the guideline set forth in the specification, paragraph bridging pages 9-10, for the term "electrostatically associated".

In the instant, the MacFarland et al. teaches the same composition as claimed. Thus, MacFarland et al. anticipates the claimed invention.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. The rejection of claim 14 under 35 U.S.C. 103(a) in view of Garcon et al. is withdrawn.

12. Claims 6, 8 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over MacFarland et al. as applied to claims 1 and 3 above, and further in view of Garcon et al.

Claim 6, which depends on claim 3, which depends on claim 1, requires the enhancement of the negative charge of the organic complex. Claim 8 depends on claim 3, which depends on claim 1. Claim 8 requires the modification of the negative and positive charge known for the organic complex and antigen, respectively.

The significance of claim 1 and 3 is provided above. And the significance of MacFarland et al. and Garcon et al. as they pertain to claims 1 and 3 is discussed above.

In the instant, while MacFarland et al. does teach the enhancement of the positive charge of the antigen, MacFarland et al. does not teach the enhancement of the negative charge of the organic complex. However, the deficiency noted of MacFarland et al. is compensated by the teachings of Garcon et al. Garcon et al. teaches the addition of charged lipid to increase the stability of liposomes, which is an organic complex. And the charged lipid that Garcon et al. teaches is a negatively charged lipid, MPL—monophosphoryl lipid A. [Lines 1-25 of page 2, in particular.]

Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to add a negatively charged lipid to the organic carrier of MacFarland et al. One of ordinary skill in the art at the time the invention was made

would have been motivated to do so to enhance the stability of the organic carrier. One of ordinary skill in the art would have had a reasonable expectation of success for doing so because enhancement of stability of organic carrier with charged lipids is well practiced in the art.

In the instant, the addition of a negatively charged lipid into the organic carrier would result in the enhancement of the carrier's overall negative charge.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory

double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 1, 3, 6-8, 12-17 and 53 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 46-55, 63-64, 67-76 and 85 of copending Application No. 10/622470, for reason(s) of record. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

In response to the double patenting rejection set forth in the previous office action, Applicant submits the intention to defer any argument or corrective action concerning the rejection.

Applicant's intention is noted. However, until the rejection is properly addressed, the rejection is maintained.

Conclusion

15. No claims are allowed.

16. The instant office action is made Non-Final.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey S. Parkin, Ph.D.
Primary Patent Examiner
Art Unit 1648

E.Le